

Simvastatin as a neuroprotective treatment for m

Submission date 19/11/2015	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 19/11/2015	Overall study status Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 21/12/2023	Condition category Nervous System Diseases	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Parkinson's disease (PD) is a long-term medical condition which is caused by the gradual loss of nerve cells (neurons) in a part of the brain called the substantia nigra. These neurons are normally responsible for producing dopamine, a chemical messenger (neurotransmitter) which carries signals around the brain that help to coordinate movement. In people suffering from PD, these neurons gradually die over time, causing the level of dopamine in the brain to gradually fall. As the levels of dopamine become lower, the brain is unable to coordinate movement as effectively, causing abnormal movements such as stiffness, tremor (uncontrollable shaking) and slowness of movement (bradykinesia). Currently, PD affects more than 127,000 people in the UK alone, with a further 10,000 diagnosed each year. Unfortunately, there is no cure for PD and so current therapies are only able to help relieve the symptoms, such as by artificially replacing dopamine or preventing the body from breaking it down. These treatments ultimately fail however, as they are unable to prevent the overall loss of neurons in the brain. Neuroprotection is an area of research which aims to protect nerves from damage. Studies have shown that statins (a group of medications which lower cholesterol) are potentially neuroprotective. The way this works is still only partly understood however, and so more research is needed to find out if statins have the potential of being neuroprotective. The aim of this study is to find out whether simvastatin has potential as a neuroprotective therapy in PD.

Who can participate?

Adults aged between 40 and 90 years old who have been diagnosed with idiopathic PD (i.e. the cause is unknown), with no current or previous use of statins.

What does the study involve?

Participants are randomly allocated to one of two treatment groups. In one group, participants are given capsules of simvastatin to take orally (by mouth) for 24 months. In the other group, participants are given placebo (dummy) capsules to take orally for 24 months. At the start of the study, when they receive their medication, participants complete a number of questionnaires and motor (movement) tests (a walking test and a finger tapping test). Participants in both groups also attend a further 6 clinic visits after 1, 6, 12, 18 and 24 months, where they are asked about their health and any medication they are taking, as well as repeating the questionnaires and motor tests. For 4 of these clinic visits, the participants will be asked to attend in the 'OFF medication' state (having omitted their usual PD medication) so that the researchers can get a true picture of their disease without it being masked by their normal medication.

What are the possible benefits and risks of participating?

Participants may or may not benefit directly from taking part in the study, but by taking part they will be contributing to a study which could potentially bring future benefit to large numbers of people with PD. There are no significant risks of taking part, however participants may experience side effects from the medication (such as muscle aches and pains) and could experience pain or bruising from blood testing.

Where is the study run from?

24 NHS hospitals in England (UK)

When is the study starting and how long is it expected to run for?

January 2015 to September 2020

Who is funding the study?

1. Cure Parkinson's Trust (UK)
2. The JP Moulton Charitable Foundation (UK)

Who is the main contact?

Mr Doug Webb

Contact information

Type(s)

Public

Contact name

Mr Doug Webb

Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)

2015-000148-40

ClinicalTrials.gov (NCT)

NCT02787590

Protocol serial number

CPMS 19666

Study information

Scientific Title

Simvastatin as a neuroprotective treatment for Parkinson's disease: a double-blind, randomised, placebo-controlled futility study in patients of moderate severity

Acronym

PD STAT

Study objectives

The aim of this study is to establish whether the cholesterol-lowering drug, simvastatin, has potential as a neuroprotective therapy in Parkinson's disease.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Newcastle and North Tyneside 2 Research Ethics Committee, 12/10/2015, ref: 15/NE/0324

Study design

Double-blind placebo-controlled multi-centre randomized futility study

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Topic: Dementias and neurodegeneration; Subtopic: Parkinson's Disease; Disease: Parkinson's disease

Interventions

Participants in this study will be randomly allocated to one of two treatment groups in a 1:1 ratio:

Intervention group: Participants will receive oral simvastatin capsules to take daily for 24 months.

Control group: Participants will receive oral matched-placebo capsules to take daily for 24 months.

Trial treatment will be provided to the participants at the baseline, 1 month, 6 month, 12 month and 18 month clinic visits; the maximum supply provided will be a 6 month supply. Bottles containing 100 capsules of either 40mg simvastatin or matched placebo will be issued to the participants.

Over a 26 month period, participants in both treatment groups will attend scheduled study clinic visits, complete a number of validated assessments and receive telephone contacts.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Simvastatin

Primary outcome(s)

Patient motor skills are determined using the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS Part III) in the OFF state at 12 and 24 months.

Key secondary outcome(s)

1. The overall impact of PD on the participant is assessed using the MDS-UPDRS total score in the practically defined ON state at 12 and 24 months
2. The impact of PD on activities of daily living is assessed using the MDS-UPDRS part II subscale score in the practically defined ON state at 12 and 24 months
3. Motor skills are assessed using timed motor tests (finger tapping and timed walk test (10MWT)) in the OFF state at 12 and 24 months
4. Depression is assessed using the Montgomery and Asberg Depression Rating Scale (MADRS) at 12 and 24 months
5. Cognition is assessed using the Addenbrooke's Cognitive Assessment-III (ACE-III) at 12 and 24 months
6. The presence of the non-motor features of PD is captured using the Non-Motor Symptom assessment scale (NMSS) at 12 and 24 months
7. A PD-specific health status is assessed using the Parkinson's disease Questionnaire (PDQ-39) at 12 and 24 months
8. Changes in PD medication are measured by capturing a levodopa-equivalent dose (LED) at 12 and 24 months
9. Cholesterol levels are captured using total, HDL, LDL, and total/HDL ratio results at 12 and 24 months
10. The presence of PD-specific pain is captured using the King's PD pain scale (KPPS) at 12 and 24 months
11. A current overall health status is captured using the EuroQoL 5D-5L (EQ-5D-5L) health status questionnaire at 12 and 24 months
12. The safety and tolerability of trial medication is assessed by adverse events (AEs) review at 12 and 24 months
13. The incidence of diabetes mellitus is assessed at 24 months using a glycated haemoglobin (HbA1c) level of 6.5% (48mmol/mol) as diagnostic of diabetes mellitus (WHO 2011)

Completion date

30/09/2020

Eligibility

Key inclusion criteria

1. Diagnosis of idiopathic PD
2. Modified Hoehn and Yahr stage \leq 3.0 in the ON medication state
3. Age 40-90 years
4. On dopaminergic treatment with wearing-off phenomenon
5. Able to comply with study protocol and willing to attend necessary study visits

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

40 years

Upper age limit

90 years

Sex

All

Total final enrolment

235

Key exclusion criteria

1. Diagnosis or suspicion of other cause for parkinsonism
2. Known abnormality on CT or MRI brain imaging considered to be causing symptoms or signs of neurological dysfunction, or considered likely to compromise compliance with study protocol
3. Concurrent dementia defined by MoCA score <21
4. Concurrent severe depression defined by MADRS score >31
5. Prior intracerebral surgical intervention for PD including deep brain stimulation, lesional surgery, growth factor administration, gene therapy or cell transplantation
6. Already actively participating in a research study that might conflict with this trial
7. Prior or current use of statins as a lipid lowering therapy
8. Intolerance to statins
9. Untreated hypothyroidism
10. End stage renal disease (creatinine clearance <30 mL/min) or history of severe cardiac disease (angina, myocardial infarction or cardiac surgery in preceding two years)
11. eGFR <30 mL/min
12. History of alcoholism or liver impairment
13. Creatine kinase (CK) >1.1 x upper limit of normal (ULN)
14. Aspartate transaminase (AST) or alanine transaminase (ALT) >1.1 x ULN
15. Females who are pregnant or breast feeding or of child-bearing potential and unwilling to use appropriate contraception methods whilst on trial treatment
16. Currently taking any medication contraindicated with simvastatin use
17. Any requirement for statin use
18. Regular participation in endurance or high -impact sports
19. Unable to abstain from consumption of grapefruit -based products

Date of first enrolment

01/12/2015

Date of final enrolment

31/03/2018

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Royal Cornwall Hospital

2 Penventinnie Lane

Treliske

Cornwall

United Kingdom

TR1 3LQ

Study participating centre

Derriford Hospital

Derriford Road

Plymouth

United Kingdom

PL6 8DH

Study participating centre

Musgrove Park Hospital

Parkfield Drive

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United Kingdom

TA1 5DA

Study participating centre

Yeovil District Hospital

Higher Kingston

Yeovil

United Kingdom

BA21 4AT

Study participating centre

Christchurch Hospital

Fairmile Road

Christchurch

United Kingdom
BH23 2JX

Study participating centre
Royal United Hospital Bath
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
St Peter's Hospital
Guildford Road
Chertsey
United Kingdom
KT16 0PZ

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Queen's Hospital
Rom Valley Way
Romford
United Kingdom
RM7 0AG

Study participating centre

John Radcliffe Hospital

Headley Way
Oxford
United Kingdom
OX3 9DU

Study participating centre**Luton and Dunstable University Hospital**

The L&D Hospital NHS Foundation Trust
Lewsey Road
Luton
United Kingdom
LU4 0DZ

Study participating centre**Addenbrookes Hospital**

Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre**Salford Royal Hospital**

Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre**Fairfield General Hospital**

Rochdale Old Road
Bury
United Kingdom
BL9 7TD

Study participating centre**Royal Preston Hospital**

Sharoe Green Lane North
Preston
United Kingdom
PR2 9HT

Study participating centre

Leeds General Infirmary

Great George Street

Leeds

United Kingdom

LS1 3EX

Study participating centre

Clinical Ageing Research Unit

Campus for Ageing and Vitality

Newcastle upon Tyne

United Kingdom

NE4 5PL

Study participating centre

Royal Devon and Exeter Hospital

Barrack Road

Exeter

United Kingdom

EX2 5DW

Study participating centre

King's College Hospital

Denmark Hill

Brixton

London

United Kingdom

SE5 9RS

Study participating centre

Royal Hallamshire Hospital

Glossop Road

Sheffield

United Kingdom

S10 2JF

Study participating centre

Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Rotherham General Hospital
Moorgate Road
Rotherham
United Kingdom
S60 2UD

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-Trent
United Kingdom
ST4 6QG

Sponsor information

Organisation
Plymouth Hospitals NHS Trust

ROR
<https://ror.org/05x3jck08>

Funder(s)

Funder type
Charity

Funder Name
Cure Parkinson's Trust

Funder Name
The JP Moulton Charitable Foundation

Results and Publications

Individual participant data (IPD) sharing plan

The researchers intend to deposit anonymised patient-level data in the Critical Path for Parkinson's Consortium.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		31/10/2022	01/11/2022	Yes	No
Protocol article	protocol	07/10/2019	23/07/2020	Yes	No
Basic results		03/06/2021	16/06/2022	No	No
HRA research summary			28/06/2023	No	No
Protocol (other)		31/10/2022	21/12/2023	No	No
Statistical Analysis Plan		24/08/2020	07/01/2022	No	No
Statistical Analysis Plan		31/10/2022	21/12/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes